

1. (Amended) A non-human transgenic animal having a transgene comprising a polynucleotide sequence encoding a fusion protein which inhibits transcription in eukaryotic cells, the fusion protein comprising a first polypeptide which is a Tet repressor or mutated Tet repressor that binds to a *tet* operator sequence, operatively linked to a heterologous second polypeptide which inhibits transcription in eukaryotic cells.

2. (Amended) The animal of claim 1, wherein the first polypeptide of the fusion protein is a Tet repressor that binds to *tet* operator sequences in the absence but not the presence of tetracycline or a tetracycline analogue.

3. (Amended) The animal of claim 2, wherein the first polypeptide comprises an amino acid sequence shown in SEQ ID NO: 17.

4. (Amended) The animal of claim 1, wherein the first polypeptide of the fusion protein is a mutated Tet repressor that binds to *tet* operator sequences in the presence but not the absence of tetracycline or a tetracycline analogue.

5. (Amended) The animal of claim 5, wherein the mutated Tet repressor has at least one amino acid substitution compared to a wild-type Tet repressor.

6. (Amended) The animal of claim 7, wherein the mutated Tet repressor has an amino acid substitution at least one amino acid position corresponding to an amino acid position selected from the group consisting of position 71, position 95, position 101 and position 102 of a wild-type Tn10-derived Tet repressor amino acid sequence.

7. (Amended) The animal of claim 8, wherein the mutated Tet repressor comprises an amino acid sequence shown in SEQ ID NO: 19.

8. (Amended) The animal of claim 1, wherein the second polypeptide comprises a transcription silencer domain of a protein selected from the group consisting of v-erbA, the Drosophila Krueppel protein, the retinoic acid receptor alpha, the thyroid hormone receptor alpha, the yeast Ssn6/Tup1 protein complex, the Drosophila protein even-skipped, SIR1, NeP1, the Drosophila dorsal protein, TSF3, SFI, the Drosophila hunchback protein, the Drosophila knirps protein, WT1, Oct-2.1, the Drosophila engrailed protein, E4BP4 and ZF5.

D 3 11. (Amended) The animal of claim 1, further having a second transgene comprising a gene of interest operably linked to at least one *tet* operator sequence.

D 4 13. (Amended) The animal of claim 1, which is selected from a group consisting of a cow, a goat, a sheep and a pig.

14. (Amended) A method for modulating transcription of the second transgene in the transgenic animal of claim 11, comprising administering tetracycline or a tetracycline analogue to the animal.

D 5 15. (Amended) A non-human transgenic animal having a transgene comprising a polynucleotide sequence encoding a fusion protein which inhibits transcription in eukaryotic cells, the fusion protein comprising a first polypeptide which is a Tet repressor or a mutated Tet repressor that binds to a *tet* operator sequence, operatively linked to a heterologous second polypeptide which inhibits transcription in eukaryotic cells, wherein the transgene is integrated by at a predetermined location within a chromosome within cells of the animal.

16. (Amended) The animal of claim 15, wherein the first polypeptide of the fusion protein is a Tet repressor that binds to *tet* operator sequences in the absence but not the presence of tetracycline or a tetracycline analogue.

D 6 18. (Amended) The animal of claim 16, wherein the first polypeptide comprises an amino acid sequence shown in SEQ ID NO: 17.

D 7 19. (Amended) The animal of claim 16, wherein the first polypeptide of the fusion protein is a mutated Tet repressor that binds to *tet* operator sequences in the presence but not the absence of tetracycline or a tetracycline analogue.

D 8 21. (Amended) The animal of claim 19, wherein the mutated Tet repressor has at least one amino acid substitution compared to a wild-type Tet repressor.

D 9 22. (Amended) The animal of claim 21, wherein the mutated Tet repressor has an amino acid substitution at least one amino acid position corresponding to an amino acid

position selected from the group consisting of position 71, position 95, position 101 and position 102 of a wild-type Tn10-derived Tet repressor amino acid sequence.

23. (Amended) The animal of claim 22, wherein the mutated Tet repressor comprises an amino acid sequence shown in SEQ ID NO: 19.

24. (Amended) The animal of claim 15, wherein the second polypeptide comprises a transcription silencer domain of a protein selected from the group consisting of v-erbA, the Drosophila Krueppel protein, the retinoic acid receptor alpha, the thyroid hormone receptor alpha, the yeast Ssn6/Tup1 protein complex, the Drosophila protein even-skipped, SIR1, NeP1, the Drosophila dorsal protein, TSF3, SFI, the Drosophila hunchback protein, the Drosophila knirps protein, WT1, Oct-2.1, the Drosophila engrailed protein, E4BP4 and ZF5.

25. (Amended) The animal of claim 15, further having a second transgene comprising a gene of interest operably linked to at least one *tet* operator sequence.

26. (Amended) A method for modulating transcription of the second transgene in the transgenic animal of claim 25, comprising administering tetracycline or a tetracycline analogue to the animal.

27. (Amended) A non-human transgenic animal having a transgene integrated into the genome of the animal and also having a *tet* operator-linked gene in the genome of the animal, wherein:

the transgene comprises a transcriptional regulatory element functional in cells of the animal operatively linked to a polynucleotide sequence encoding a fusion protein which inhibits transcription of said *tet* operator linked gene,

said fusion protein comprises a first polypeptide that is a Tet repressor operably linked to a heterologous second polypeptide which inhibits transcription of said *tet* operator-linked gene in eucaryotic cells,

said *tet* operator-linked gene confers a detectable and functional phenotype on the animal when expressed in cells of the animal,

said transgene is expressed in cells of the animal at a level sufficient to produce amounts of said fusion protein that are sufficient to inhibit transcription of the *tet* operator-linked gene; and

in the absence of tetracycline or a tetracycline analogue in the animal, said fusion protein binds to the *tet* operator-linked gene and inhibits transcription of the *tet* operator linked gene, wherein the level of expression of the *tet* operator-linked gene can be upregulated by administering tetracycline or a tetracycline analogue to the animal.

28. (Amended) A non-human transgenic animal having a transgene integrated into the genome of the animal and also having a *tet* operator-linked gene in the genome of the animal, wherein:

the transgene comprises a transcriptional regulatory element functional in cells of the animal operatively linked to a polynucleotide sequence encoding a fusion protein which inhibits transcription of said *tet* operator linked gene,

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said fusion protein comprises a first polypeptide that is a mutated Tet repressor that binds to *tet* operator sequences in the presence, but not the absence, of tetracycline or a tetracycline analogue, operably linked to a heterologous second polypeptide which inhibits transcription of said *tet* operator-linked gene in eucaryotic cells,

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said *tet* operator-linked gene confers a detectable and functional phenotype on the animal when expressed in cells of the animal,

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said transgene is expressed in cells of the animal at a level sufficient to produce amounts of said fusion protein that are sufficient to inhibit transcription of the *tet* operator-linked gene; and

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in the presence of tetracycline or a tetracycline analogue in the animal, said fusion protein binds to the *tet* operator-linked gene and inhibits transcription of the *tet* operator linked gene, wherein the level of expression of the *tet* operator-linked gene can be upregulated by depleting tetracycline or a tetracycline analogue from the animal.